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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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QUARLES & BRADY LLP
FIRSTAR PLAZA, ONE SOUTH PINCKNEY STREET
P.O BOX 2113 SUITE 600
MADISON, WI 53701-2113

| EXAMINER | |
|---|---|
| CHUNDURU, SURYAPRABHA | |
| **ART UNIT** | **PAPER NUMBER** |
| 1637 | |

DATE MAILED: 11/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/719,168 | DAHL ET AL. | |
| | Examiner | Art Unit | |
| | Suryaprabha Chunduru | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *30 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *84-147* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *84-147* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/21/06, 8/23/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election without traverse of Group I (claims 1-32, and 37-80) in the reply filed on August 30, 2006 is acknowledged.

### *Status*

2. The amendment filed along with the election is considered. Claims 1-83 are cancelled by the amendment. New claims 84-147 represent the elected claims in Group I and are considered for examination in this office action.

### *Priority*

3. This application filed on November 21, 2003 claims benefit of US provisional application 60/428,013 filed on 11/21/2002.

### *Information Disclosure Statement*

4. The Information Disclosure Statement filed on August 21, 2006 and August 23, 2006 have been entered and considered.

### *Informalities*

5. The following informalities are noted during the examination:

(i) in abstract line 1, "kits" is repeated twice. A typographical error.

(ii) claims 106-108 recite 'further comprising step l)', should have been step k).

(iii) claim 147 recites 'further comprising the step of: e), should have been step of : f).

Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 104-120 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 104 recites the limitation "the single-stranded DNA" in step c). There is insufficient antecedent basis for this limitation in the claim because the preceding step (a) recites DNA which is not necessarily a single-stranded DNA, instead it could be a double-stranded nucleic acid. Thus the recitation of 'the single-stranded DNA' lacks support.

***Claim Rejections - 35 USC § 102***

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

A. Claims 84-89, 91, 96-97, 100-109, 114-115, 118-126, 133-138, 140-147 are rejected under 35 U.S.C. 102(b) as being anticipated by Kurn et al (US 6,251,639).

Kurn et al. teach a method of 84, 104, 106, 122, for amplifying a target nucleic acid sequence, wherein the method comprises

(a) hybridizing a riboprimer (composite primer comprising RNA and DNA portion) to a DNA template comprising target nucleic acid sequence (see col. 4, line 28-33);

(b) extending the riboprimer with a DNA polymerase (see col. 4, line 37-38);

(c) cleaving the annealed riboprimer to the template and repeats primer extension, whereby multiple copies of the complementary sequence of the target nucleic acid are produced (see col. 4, line 38-44).

With regard to claim 85, 105, Kurn et al. teach that the method further comprises, prior to step (b), hybridizing a blocking oligonucleotide (termination polynucleotide sequence) to a region of the template that is 5' with respect to the hybridization of the riboprimer to the template (see col. 4, line 34-37).

With regard to claim 86, Kurn et al teach that the method is conducted under isothermal conditions (see col. 4, line 37-44, col. 11, line 64-67, col. 12, line 1-9).

With regard to claim 87-88, 146-147, Kurn et al. teach that he method further comprises attaching multiple copies produced in step c) onto a solid support to make a microarray and also comprises a step of hybridizing multiple copies produced in step c) to oligonucleotide probe arrays (see col. 39, line 36-67, col. 40, line 1-13).

With regard to claim 89, Kurn et al. teach that the step b) comprises utilization of at least one type of labeled dNTP such that labeled extension products are generated (col. 5, line 50-67, col. 6, line 1-3).

With regard to claim 91, 109, 125-126, 145, Kurn et al. teach that the method utilizes one or more (plurality) of riboprimers (see col. 5, line 4-5, col. 8, line 29-47, col. 20, line 66-67).

With regard to claim 96-97, 114-115, 133, Kurn et al. teach that the 5'-end portion of the riboprimer is not complementary to the target nucleic acid sequence, which can be copied by a second-primer extension (see col. 17, line 38-43, col. 10, line 22-45, col. 30, line 36-67).

With regard to claims 100-103, 118-121, 123-124, 135-138, Kurn et al. teach that the DNA polymerase is selected from the group consisting of Bst DNA polymerase and RNase H enzyme is thermostable RNase H (see col. 26, line 13-21, col. 50, line 11).

With regard to claim 104, 122, 141, Kurn et al. teach obtaining DNA comprising a target nucleic acid, obtaining a riboprimer, annealing the riboprimer to the target DNA, obtaining a strand-displacing DNA polymerase, extending riboprimer annealed to the DNA, obtaining the double-stranded complex, contacting the double-stranded complex with RNase H, annealing a second rib primer, extending the extension product and obtaining a second primer extension product (see col. 10, line 22-45, col. 36, line 58-61, col. 43, line 1-67, col. 44, line 1-67, col. 45, line 1-13).

With regard to claims 107-108, Kurn et al. teach detecting and quantization primer extension products (see col. 45, line 14-67, col. 46, line 1-5, col. 53, line 16-27).

With regard to claim 122, 142-144, Kurn et al. teach generating multiple copies of a polynucleotide sequence complementary to an RNA sequence with a RNA-dependent DNA polymerase (see col. 11, line 52-56, col. 33, line 49-63, col. 36, line 58-61, col. 31, line 10-36).

With regard to claim 134, Kurn et al. teach that the target RNA is mRNA (see col. 33, line 49-52).

With regard to claim 140, Kurn et al. teach that the enzyme that cleaves RNA in step b) cleaves RNA from RNA/DNA hybrid (see col. 34, line 25-26). Accordingly the instant claims are anticipated by Kurn et al.

B. Claims 84, 86-95, 98, 100-104, 106-113, 116, 118-132, 134-147 are rejected under 35 U.S.C. 102(b) as being anticipated by Dean et al (US 6,977,148).

Dean et al. teach a method of 84, 104, 106, 122, for amplifying a target nucleic acid sequence, wherein the method comprises

(a) hybridizing a riboprimer (composite primer comprising RNA and DNA portion or RNA type primer) to a DNA / RNA template comprising target nucleic acid sequence (see col. 2, line 29-67, col. 3, line 1-9, col. 34, line 36-67);

(b) extending the riboprimer with a DNA polymerase (see col. 2, line 29-67, col. 34, line 36-51);

(c) cleaving the annealed riboprimer to the template and repeats primer extension, whereby multiple copies of the complementary sequence of the target nucleic acid are produced (see col. 34, line 36-67, col. 36, line 10-51).

With regard to claim 86, Dean et al. teach that the method is conducted under isothermal conditions (see col. 30, line 60-67, col. 31, line 1-14).

With regard to claim 87-88, 146-147, Dean et al. teach that the method further comprises attaching multiple copies produced in step c) onto a solid support to make a microarray and also comprises a step of hybridizing multiple copies produced in step c) to oligonucleotide probe arrays (see col. 33, line 45-58).

With regard to claim 89, Dean et al. teach that the step b) comprises utilization of at least one type of labeled dNTP such that labeled extension products are generated (col. 31, line 41-67, col. 32, line 1-67).

With regard to claim 91, 109, 125-126, 145, Dean et al. teach that the method utilizes multiple (plurality) riboprimers (see col. 33, line 45-50, col. 65, line 15-21).

With regard to claims 90, 92-95, 98, 110-113, 116, 127-132, 139, Dean et al. teach that the riboprimer comprises random sequences, or entirely made up of ribonucleotides, 3' end of the primer complementary to the target nucleic acid sequence, or primer comprises modified nucleotides which include 2' deoxy modifications (see col. 2, line 43-67, col. 3, line 1-9, col. 9, line 27-67, col. 10, line 1-67, col. 11, line 1-67, col. 12, line 1-67, col. 13, line 1-19).

With regard to claims 100-103, 118-121, 123-124, 135-138, Dean et al. teach that the DNA polymerase is selected from the group consisting of bacteriophage ϕ29 DNA polymerase Exo (-) Bst DNA polymerase, and RNase H enzyme is thermostable RNase H (see col. 29, 12-54).

With regard to claims 107-108, Dean et al. teach detecting and quntitating primer extension products (see col. 35, line 22-60col. 37, line 9-25).

With regard to claim 122, 141-144, Dean et al. teach generating multiple copies of a polynucleotide sequence complementary to an RNA sequence with a RNA-dependent DNA polymerase (see col. 34, line 10-67, col. 35, line 1-22).

With regard to claim 134, Dean et al. teach that the target RNA is mRNA (see col. 34, line 35-51).

With regard to claim 140, Dean et al. teach that the enzyme that cleaves RNA in step b) cleaves RNA from RNA/DNA hybrid (see col. 34, line 35-51). Accordingly the instant claims are anticipated by Dean et al.

***Claim Rejections - 35 USC § 103***

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 99, 117 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kurn et al. (US . 6,251,639) in view of Berg et al. (US 5,837,459).

Kurn et al. teach a method for amplifying a target nucleic acid sequence suing riboprimers as discussed above in section 7A.

However, Kurn et al. did not teach blocking oligo comprising peptide nucleic acid analog.

Berg et al. teach a method for generating RNA transcripts, wherein the method uses a peptide nucleic acid (PNA) blocking oligonucleotide (see col. 5,line 59-67). Berg et al. also teach that the PNA blocks the transcription from initiation site so as to produce equal length transcripts, terminating at random sites down stream from the initiation site leading to long transcription products of varying lengths (see col. 2, line 30-37).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the method for amplifying a nucleic acid target sequence using riboprimers as disclosed by Kurn et al. in a manner of as taught by Berg et al. with the use of PNA blocking oligo nucleotide for the purpose of blocking the transcription at random sites from the transcription initiation sites to obtain long transcription products of varying lengths because Berg et al. explicitly taught that that the PNA blocks the transcription from initiation site so as to produce equal length transcripts, terminating at random sites down stream from the initiation site leading to long transcription products of varying lengths (see col. 2, line 30-37). An ordinary artisan would have a reasonable expectation of success that inclusion of the said PNA blocking oligo would result in blocking transcription at random sites and obtaining long transcripts of varying lengths and such modification of the method would be obvious over the cited prior art in the absence of secondary considerations.

***Conclusion***

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M , Mon - Friday,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Suryaprabha Chunduru
Primary Examiner
Art Unit 1637

Prabha Chunduru
SURYAPRABHA CHUNDURU 11/02/06
PATENT EXAMINER